numerical data suggest a plateauing or even slight decrease in the length of unaffected nail in the itraconazole group. In contrast to Buck, however, we think that there is a continuous increase in the terbinafine group. We are confident that our opinion will be supported by the statistical evaluation of an additional, blinded 24 week follow up that we have performed in patients with clinical cure or continuous clinical improvement at 52 weeks.

Buck's letter gives us the opportunity to comment on rates of relapse. De Cuyper recently reported that after 16 weeks' treatment with terbinafine and 32 weeks' follow up 17 patients who had been treated effectively were observed for a further two years; relapse occurred in only three.¹ This result accords with the 18% recurrence rate 12 months after clinical and mycological cure of the toenails with terbinafine reported by Villars and Jones.² The relatively high proportion of patients with adverse events in our study (40%) should not be overemphasised. In another study of onychomycosis with similar methodological conditions adverse events occurred in 41% of the patients taking placebo for 12 weeks.³ In our study more than 90% of the patients and doctors stated that the tolerability of both drugs was good or excellent. We believe that terbinafine provides more than short term benefit for most patients.

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Surgical bleeding and calcium antagonists

EDITOR,—L E Wagenknecht and colleagues have reported the use of nimodipine, a dihydropyridine calcium antagonist, in 149 patients undergoing replacement of a cardiac valve.¹ In a randomised, placebo controlled, double blind clinical trial nimodipine (30 mg started 12 hours before surgery and given four times a day for five days) increased major bleeding. Although patients scheduled for cardiac surgery commonly receive calcium antagonists until the operation as part of their long term cardiovascular treatment,² Wagenknecht and colleagues' finding raises the possibility that calcium antagonists may result in these patients

having an increased bleeding diathesis. We therefore reanalysed the data on postoperative bleeding and blood transfusion from our studies in patients scheduled for elective coronary artery bypass grafting.³⁻⁵

Our four trials were conducted in a prospective randomised fashion in a total of 120 patients. Patients with a history of a coagulation disorder and those who had received anticoagulants or aspirin within five days of the operation were excluded. On the morning of surgery the patients received their usual long term drug treatment, including calcium antagonists. Anaesthesia and cardiopulmonary bypass techniques were standardised. Until the first postoperative morning the blood loss through chest drains was measured systematically and the haemoglobin loss through the drains was calculated. During and after the operation a strict protocol was applied to the transfusion of blood products and fluid treatment. Differences between the groups were tested with the *t* test and Mann-Whitney U test.

Of the 81 patients receiving long term treatment with calcium antagonists, 38 received nifedipine and 35 diltiazem, while the eight others were taking verapamil, nisoldipine, amlodipine, or felodipine. No patient received nimodipine. When the patients who were receiving long term treatment with calcium antagonists were compared with those who were not there was no difference in postoperative blood loss through the chest drains, haemoglobin loss, or red cell transfusions (table 1).

In Wagenknecht and colleagues' study two of the three patients treated with nimodipine who died of blood loss had a pre-existing coagulopathy. We excluded patients with pre-existing coagulation disorders from our studies. The increased bleeding reported by Wagenknecht and colleagues may be related specifically to nimodipine or to their population of patients (that is, those undergoing replacement of a cardiac valve). Clearly, the possibility that calcium antagonists increase the tendency to bleeding in patients having cardiac surgery requires further studies.

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Table 1—Blood and haemoglobin loss through chest drains and units of red cells transfused in 120 patients undergoing coronary artery bypass grafting. Figures are means (95% confidence intervals)

Patients receiving calcium antagonists	Postoperative blood loss (ml)	Postoperative haemoglobin loss (g)	Red cells transfused (units)	
			During operation	After operation
Yes (n=81)	1010 (927 to 1092)	56 (49 to 63)	0.7 (0.5 to 1.0)	0.6 (0.4 to 0.8)
No (n=39)	1041 (933 to 1150)	62 (52 to 73)	0.6 (0.3 to 0.9)	0.8 (0.5 to 1.1)

Insulin dependent diabetes mellitus in twins

Differences between monozygotic and dizygotic twins may need to be taken into account

EDITOR,—In their study of diabetic twins Kirsten O Kyvik and colleagues fail to take into account the fact that half of dizygotic but no monozygotic twins are of different sex.¹ They give no reference to indicate whether the incidence and age at onset of diabetes are the same or different in boys and girls—a common omission in such studies. Moreover, the assumption that differences in the incidence of a disease between monozygotic twins and between dizygotic twins are measures of the influence of environment and heredity, respectively, should not go unquestioned, since the important environmental factors are likely to be infection and diet, both of which may interact with constitutional factors—for example, autoimmune reactions are quite likely to be related both to sex and to the nature of the immune response.

Nor can we be sure that monozygotic twins are reared in the same way as are dizygotic twins or are of the same modal birth weight, with all the implications that Barker has pointed out.² Certainly the mothers of dizygotic twins tend to be older and more commonly multiparous. Does it matter anyway, given that all disease involves both nature and nurture (even homozygous people with phenylketonuria do well when given a diet low in phenylalanine)?

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Authors' reply

EDITOR,—We did not do a separate analysis of concordance in twin pairs of the opposite and the same sex because we had no prior reasons to do so. In our twin series the mean age at onset of diabetes mellitus is 14.3 years for females and 19.4 years for males ($P=0.144$) among the monozygotic twins and 10.5 years for females and 15.0 years for males ($P=0.021$) among the dizygotic twins. This agrees with the well established epidemiological evidence that the onset is slightly earlier in girls than boys owing to an earlier prepubertal incidence peak in girls. Figure 1 shows the Kaplan-Meier estimates of the individual risk of disease in our twins, according to zygosity and sex. As expected, females have a slightly increased risk early in life,

Fig 1—Estimated risk of disease in individual twins, according to zygosity and sex